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Hematology and Biochemistry of Small Mammals

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SMALL MAMMAL HEMATOLOGY

Blood cell morphology of small mammals resembles that of domestic animals. However, establishing representative population-based hematologic reference intervals (RIs) is difficult because of the limited numbers of healthy individuals within studies, intra-species variations (age, breed, sex, diet, reproductive status), and variations in blood collection techniques and laboratory procedures.^{11,78} Therefore RIs should be used as a tool rather than a sole guide for result interpretation.¹³ Hematologic parameters derived from inadequate RIs may yield false-positive or false-negative results.⁴³ Using values from a single individual (subject-based; see Biochemistry below) to establish health and to help detect a pathologic state may be valuable for some small mammal species in which having large sample of individuals for RI studies is not feasible.^{14,78}

Blood Collection and Handling

Blood collection techniques and handling are described in various chapters of this publication and other references.^{10,11,80} Because of the small sample volume that can be obtained from one animal, a single lithium heparin (anticoagulant) microtainer tube is generally used in small mammals to perform both hematologic and biochemical testing.⁸¹ Ideally, blood smears should be made from blood without added anticoagulants.⁸⁰ Additionally, submitting a properly made blood smear at the time of venipuncture prevents artifacts related to *in vitro* aging of blood cells.

General Hematologic Features of Small Mammals

Evaluation of Erythrocytes

Erythrocytes of mammals are small, anucleated, and biconcave (discocytes) cells that function to carry hemoglobin.³³ The red

blood cell (RBC) life span also varies and correlates positively with the species longevity and body mass. Thus small mammals have shorter RBC life spans when compared with larger species because of higher rates of oxidative metabolism.¹⁵

Rats and Mice. Hematologic parameters and reference intervals of mice and rats are influenced by many preanalytic factors such as strain, sex, age, exercise, circadian cycle, and nutrition.^{2,3,43} Reference intervals for mice and rats are available in this textbook and other publications.^{13,64,76}

Mature erythrocytes of rats and mice are round and biconcave with central pallor and a diameter between 5 to 7 μm .⁶⁴ Polychromasia (proportion of erythrocytes that stain more basophilic than mature erythrocytes) and anisocytosis are pronounced because of the high numbers of reticulocytes (2%–7% in adults, 10%–20% in young), which is directly related to the short erythrocyte half-life of 45 to 60 days for rats and 40 to 50 days for mice.^{10,11} Low numbers of Howell Jolly bodies (nuclear chromatin remnants) and nucleated RBCs are common in normal rats and mice.^{46,64} Rouleaux formation (stack-of-coins of RBCs) is rarely seen, even with inflammatory disease.¹⁰

Hamsters and Gerbils. The golden or Syrian hamster is the most popular research and pet hamster. Hematologic values of hamsters and gerbils can be found in this textbook and other publications.^{36,49,64} While castration lowers the RBC count by 25% to 30% because of testosterone decrease, pseudohibernation in the hamster causes the red cell mass to increase because of prolongation of the erythrocyte life span.^{36,46} Polychromatophilic cells and basophilic stippling are common in young and adult gerbils, likely because of the shorter erythrocyte life span (RBC half-life, 9–10 days) compared with that of other laboratory rodents.^{3a,49} As in other rodents, RBC concentration is higher in males than in females.⁸⁰ Gerbils less than 8 weeks old have a red cell mass of less than 50% of the adult value and larger erythrocytes.³⁶

Guinea Pigs. Guinea pigs have larger erythrocytes and a lower RBC count than do other small mammals.⁸⁰ Unlike other rodents, hematologic sex differences are not reported, and rouleaux formation is normally seen on blood smears.⁴⁹ Reference values are reported in this text and from other references.^{80,84,86}

Chinchillas. Hematologic features of chinchillas resemble those of rats and mice.⁶² Affinity of hemoglobin for oxygen is higher in chinchillas than in other rodents and rabbits, likely as an adaptation to their natural high-altitude environment.⁵⁷

Rabbits. In contrast to rodents, erythrocyte parameters do not differ significantly between male and female rabbits.⁸⁰ Polychromatophilic erythrocytes as well as a few nucleated red cells and occasional Howell Jolly bodies (basophilic nuclear remnants) are seen in blood smears because of the high erythrocyte turnover rate.⁵⁰ Likewise, high numbers of circulating reticulocytes are present in adult (2%–4%) and

young (3%–11%) rabbits.^{53,80} Normal hematologic parameters are reported in this and other publications.^{50,53,80}

Ferrets. Hematologic reference values of adult ferrets are similar to those of dogs and cats except for higher hematocrit values, hemoglobin concentration, and RBC and reticulocyte counts.^{24,72} Inhalant anesthesia in ferrets may significantly and rapidly decrease the RBC mass because of splenic sequestration and hypotension.¹¹ Normal hematologic values have been reported for ferrets.^{23,69,83,85}

Hedgehogs. There are minimal data from healthy African hedgehogs to establish true reference intervals.^{35,56a} Values (mean and standard deviation) of a mixed population of healthy and ill animals have been published.³⁹ High numbers of nucleated RBCs, Howell Jolly bodies, and reticulocytes were found in a study of healthy juvenile European hedgehogs.⁶⁹

Interpretation of Abnormal Erythrocyte Parameters

Most disease processes causing anemia in other species also cause anemia in small mammals. The number of circulating reticulocytes (young erythrocytes) is a useful indicator of the bone marrow's response to anemia and the most practical approach to classify anemia.³⁴ Reticulocytes stain basophilic (polychromatophilic), are larger, and contain less hemoglobin than mature erythrocytes. Therefore, if reticulocytes are present in sufficient numbers, a high mean corpuscular volume and a low mean corpuscular hemoglobin concentration are expected. However, polychromasia should not be overinterpreted, because most small mammals, especially gerbils, normally have high percentages of polychromatophilic cells due to the short erythrocyte life span.⁴⁹ Anisocytosis, basophilic stippling, and Howell-Jolly bodies are other indicators of a bone marrow response to anemia. Nucleated RBCs can be associated with regenerative responses or secondary to alterations in the blood/bone marrow barrier when reticulocytosis is not present (inappropriate metarubricytosis). In rabbits, increased numbers of nucleated RBCs have been associated with acute infectious processes, possibly related to endothelial damage and regeneration. Causes of regenerative anemia are blood loss and hemolysis, whereas nonregenerative anemia is the result of defective or decreased erythropoiesis and is nonspecific.¹¹ A maximal bone marrow response may be seen approximately 4 days after the inciting cause of hemolysis or blood loss. Therefore anemia may be initially classified as nonregenerative or prerenal until enough time has elapsed.³⁴

Interpreting the hematocrit along with the total protein concentration is also recommended. A hematocrit below the reference interval with a low total protein concentration suggests blood loss, while a mild normocytic, normochromic, nonregenerative anemia and normal total protein concentration may indicate anemia of chronic disease.

Other clinicopathologic parameters such as neutrophil count, platelet count, and total bilirubin level may provide useful information to determine the underlying cause of the anemia. In general, panleukopenia (nonregenerative anemia,

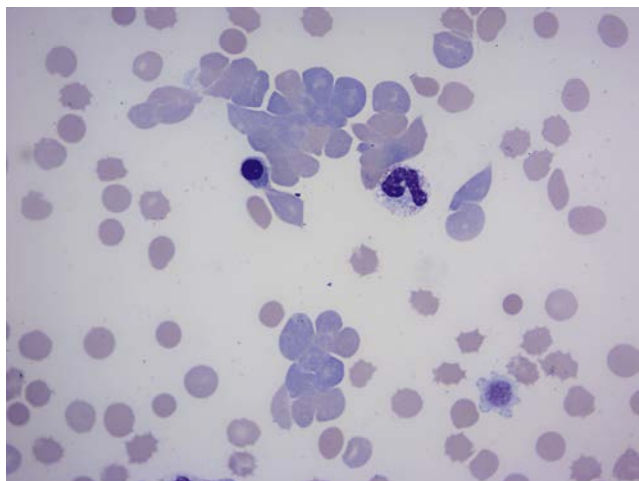


Fig. 39.1 Autoagglutination (clumping) of erythrocytes in the blood film of a guinea pig with immune-mediated hemolytic anemia. A nucleated RBC, polychromatophilic erythrocytes and a neutrophil displaying toxic change (cytoplasmic basophilia) (left to right) are present. (Wright-Giemsa, magnification $\times 100$.)

neutropenia, and thrombocytopenia) indicates bone marrow hypoplasia. In intact female ferrets, high levels of estrogen due to prolonged estrus may cause bone marrow suppression.⁷² An animal with a mild nonregenerative anemia and an inflammatory leukogram likely has anemia of chronic disease, including malignant neoplasia and infectious disease. Pasteurellosis, dental disease, pneumonia, pododermatitis, and pyometra are potential causes of anemia of chronic disease in rabbits.⁵³ Anemia of chronic inflammation may be seen in ferrets with endocrinopathy, gastrointestinal disease, neoplasia (lymphoma), and, to a lesser degree, infectious diseases.¹¹ In general, regenerative anemia and hyperbilirubinemia suggest hemolysis, whereas anemia and hypoproteinemia may indicate blood loss. Immune-mediated hemolytic anemia has been reported in laboratory rabbits with lymphoma,⁵¹ and occurs in rare cases of small mammal species in clinical practice (Fig. 39.1). Fisher rats with large granular lymphocyte leukemia may have associated immune-mediated anemia, which, as in other species, is characterized by numerous spherocytes (see below, Interpretation of Abnormal Leukocyte Parameters).¹³ A diagnosis of hemolytic anemia will grant a blood smear examination to search for erythrocytic hemoparasites.⁴⁹ However, hemoparasites are rarely seen in pet rodents.⁶²

Microcytic hypochromic regenerative anemia suggests chronic blood loss, especially due to gastrointestinal parasites (Fig. 39.2).⁴⁹ Heavy lice infestations, occasionally seen in rats and guinea pigs, can also cause chronic blood loss.⁶² Ectoparasitic and endoparasitic infestations with secondary blood loss anemia are common in wild European hedgehogs admitted in rehabilitation centers.⁶⁹ In ferrets, *Helicobacter*-associated duodenal ulcers are a common cause of regenerative anemia secondary to blood loss.^{11,23} Trauma, severe flea infestation, hematuria, bleeding uterine adenocarcinomas, and endometrial hyperplasia are causes of regenerative anemia in rabbits.^{51,53} Regenerative anemia with increased numbers of

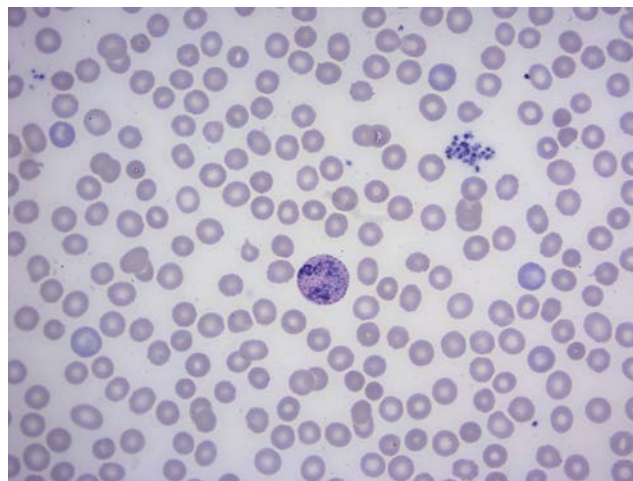


Fig. 39.2 Hypochromic erythrocytes showing increased central pallor in the blood film of a rabbit. A heterophil (middle) and a small platelet clump (top right) are also present. (Wright-Giemsa, magnification $\times 100$.)

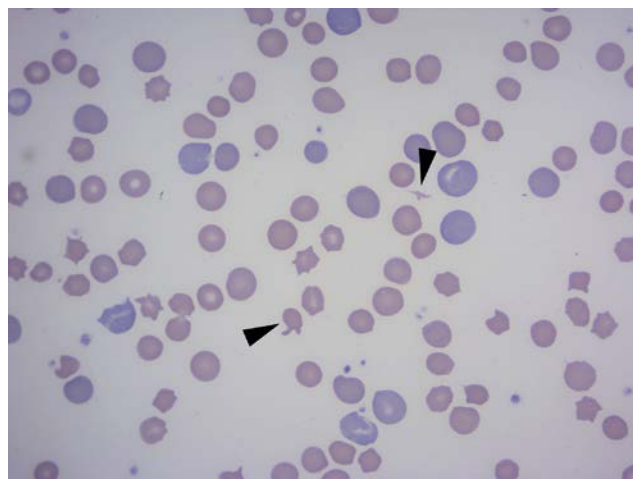


Fig. 39.3 An anisocytote (left arrowhead) (erythrocyte with unevenly spaced projections of different lengths) and schistocyte (right arrowhead) (erythrocyte fragment) in the blood film of a rabbit. (Wright-Giemsa, magnification $\times 100$.)

nucleated RBCs, hypochromasia, and basophilic stippling could suggest lead toxicosis.⁵¹

Morphologically, abnormal erythrocytes (poikilocytes) documented in domestic animals may be also observed in small mammals and are generally associated with the same physiopathologic mechanisms. For example, Heinz bodies may be seen with oxidant injury, whereas anisocytosis may be present in animals with severe liver disease (Fig. 39.3).¹³

Erythrocytosis, which is a combination of a high hematocrit, RBC count, and hemoglobin concentration, is generally relative and secondary to dehydration. A high serum protein concentration is expected.

Evaluation of Leukocytes

Leukocytes are relatively similar in appearance and function across most mammal species with some differences.¹⁷ Nevertheless,

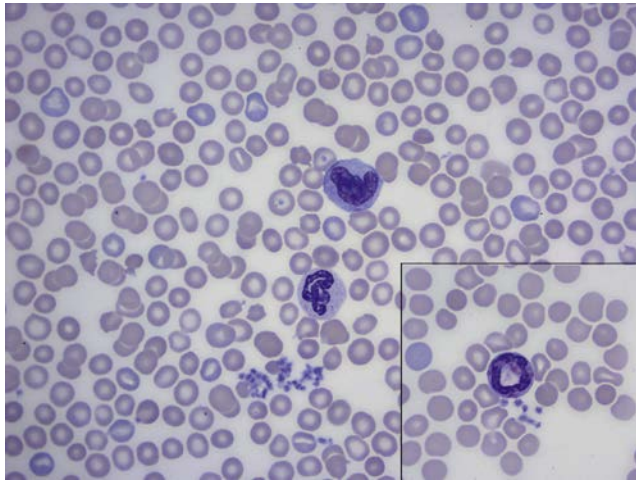


Fig. 39.4 Monocyte (top), neutrophil (bottom), and ring eosinophil (insert) in the blood film of a rat. (Wright-Giemsa, magnification $\times 100$.)

numbers, composition, and staining properties of neutrophil granules vary between species. Basophils are very uncommon in rats, mice, and hamsters but may account for up to 30% of rabbit leukocytes.⁵³ Evaluation of leukocytes should include a total white blood cell (WBC) count, as well as a differential count, with percentages and absolute numbers of each type of leukocyte.^{17,64}

Rats and Mice. Lymphocytes are the most common white blood cell (approximately 75%), followed by neutrophils.⁶⁴ As rodents age, the proportion of lymphocytes decreases whereas that of neutrophils increases.⁴⁶ Small or large lymphocytes with slightly increased amounts of cytoplasm and large granular lymphocytes can be present.⁶⁴ Neutrophils may have dust-like eosinophilic cytoplasmic granules.¹¹ Granulocytes of mice and rats occasionally have a doughnut-shaped, nonlobed nuclei (ring forms).⁴⁶ These ring forms may be present in normal animals but generally reflect accelerated granulopoiesis (Fig. 39.4).⁴⁶ Eosinophils comprise up to 7% of the WBC differential and contain numerous small, eosinophilic intracytoplasmic granules.¹¹

Hamsters and Gerbils. Leukocytes of hamsters and gerbils are similar in structure and proportions to those of rats and mice.¹¹ In hamsters, lymphocytes, predominately small with fewer large forms, are the main leukocyte, comprising 60% to 80% of the WBCs. The leukocyte count decreases to 2500 cells/ μL in Syrian hamsters during pseudohibernation.¹¹ A nocturnal increase in the WBC count and proportions of neutrophils has been observed.¹¹ Neutrophils in hamsters are frequently referred to as *heterophils* and resemble eosinophils because of eosinophilic rounded or rod-shaped cytoplasmic granules.^{11,46} Hamster eosinophils normally are seen in very low numbers and contain rod-shaped rather than rounded granules present in other rodents.⁴⁶ In gerbils, lymphocyte numbers are higher in males than in females, resulting in a 6:1 lymphocyte to heterophil ratio.³⁶

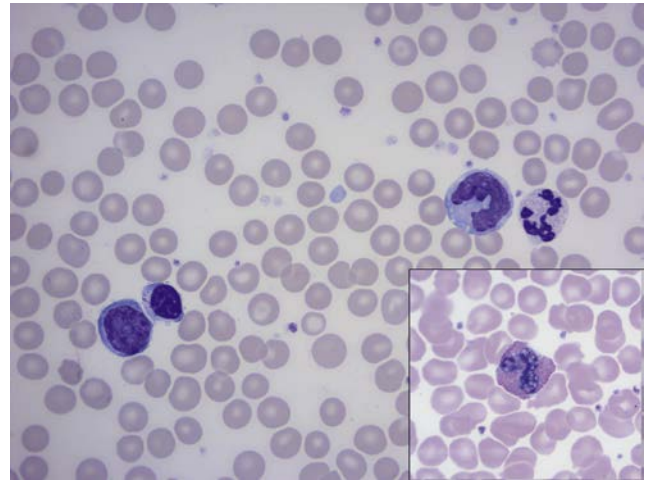


Fig. 39.5 Two lymphocytes (large and small), monocyte, and neutrophil (left to right) and eosinophil (insert) in the blood film of a guinea pig. (Wright-Giemsa, magnification $\times 1000$)

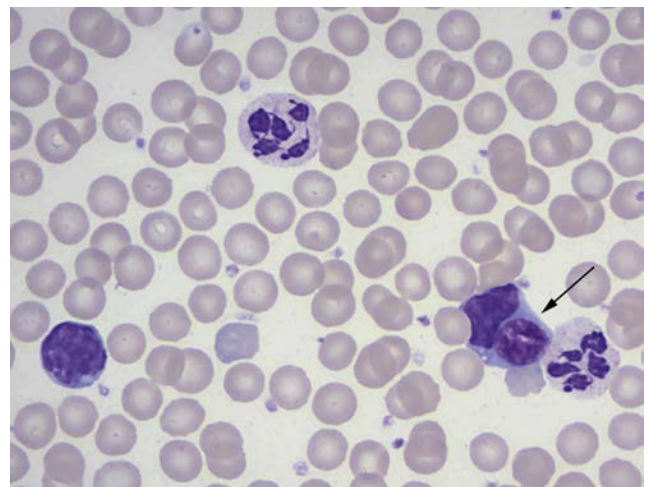


Fig. 39.6 Kurloff cell (arrow) with a large intracytoplasmic eosinophilic inclusion body in the blood smear of a guinea pig. A lymphocyte (left) and two heterophils (middle and bottom right) are also present. (Wright-Giemsa, magnification $\times 1000$)

Guinea Pigs. In normal guinea pigs, lymphocytes and fewer numbers of heterophils, the equivalent of the neutrophil in other species, comprise most of the WBCs.⁶⁶ Heterophils (pseudoeosinophils) have eosinophilic cytoplasmic granules.¹¹ Eosinophils are larger than heterophils, with less segmented nuclei and round, bright red cytoplasmic granules (Fig. 39.5).^{11,84} Small lymphocytes are more numerous than large lymphocytes, which may contain azurophilic granules.⁸⁴

The Kurloff cell is a mononuclear cell unique to guinea pigs and capybaras that contains a single large cytoplasmic inclusion body and may account for up to 3% to 4% of the leukocytes.^{11,84} The inclusion is comprised of eosinophilic, finely granular mucopolysaccharides and is located within a vacuole in the cytoplasm, displacing the nuclei (Fig. 39.6).^{11,86} Kurloff cells are seen in increased numbers in adult females, pregnant females, and in males and females after exogenous estradiol and testosterone administration.^{49,63,82} Kurloff cells have natural killer and natural cytotoxic activity.⁶³

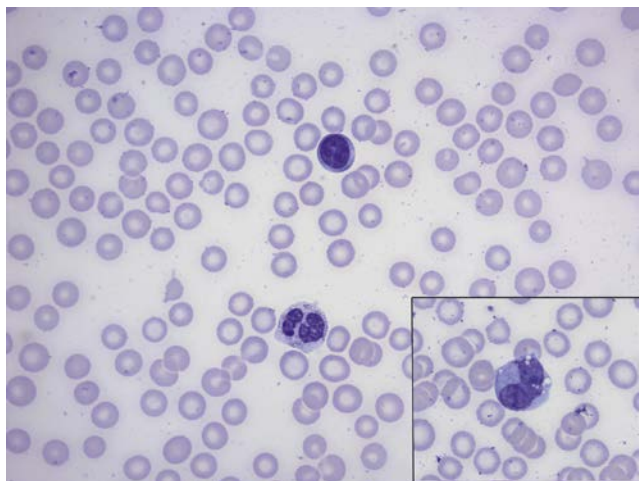


Fig. 39.7 Neutrophil with faint eosinophilic cytoplasmic granules (middle), lymphocyte (top), and monocyte (insert) in the blood smear of a chinchilla with anemia. Note hypochromic erythrocytes in the background. (Wright-Giemsa, magnification $\times 1000$)

Chinchillas. Lymphocytes are the predominant leukocyte, followed by neutrophils.⁶⁷ Mature neutrophils of chinchillas may be hyposegmented and contain faint eosinophilic cytoplasmic granules (Fig. 39.7).¹¹ Monocytes, eosinophils, and basophils are present in low numbers.⁶⁷

Rabbits. Many factors, including circadian cycles, nutrition, age, and breed, affect the WBCs of rabbits.⁵³ Leukocyte numbers are lower in newborns and juveniles younger than 6 to 12 months of age.⁶⁴ Neutrophil-to-lymphocyte proportions vary with age, from 1:2 in 2-month-old rabbits to 1:1 in adults, with the highest neutrophil numbers present in old rabbits.¹¹ Lymphocytes are reported as the predominant leukocyte.^{50,53} Most lymphocytes are small (RBC size), with occasional large lymphocytes, which occasionally display cytoplasmic azurophilic granules.^{17,51} The main granulocytes are often referred to as *heterophils* because of their large cytoplasmic granules that stain dark pink with Romanowsky stains.^{11,64} Nevertheless, rabbit heterophils are functionally equivalent to neutrophils in other mammals.¹¹ Eosinophils can be differentiated from heterophils by their larger rounded granules that tend to fill the cytoplasm and are bright red to pink-orange staining (Fig. 39.8).^{11,17,50} Unlike other mammal species, basophils are common in rabbits and may comprise up to 30% of the WBC differential but generally account for 2% to 5% of the WBCs.⁵⁰ The cytoplasm of basophils contains numerous purple to black granules (Fig. 39.9).⁶⁴

Ferrets. Hematologic parameters of ferrets are similar to other domestic carnivores, with some differences, including a slightly lower WBC count with a reference interval that ranges from 3000 to 16,700 cells/ μL .^{37,71} Neutrophils are the predominant leukocyte, with the exception of ferrets younger than 5 to 7 months, in which lymphocytes are the main leukocyte.^{11,71,85} However, in a recent study of 111 healthy ferrets, lymphocytes comprised 53% of the WBC differential,

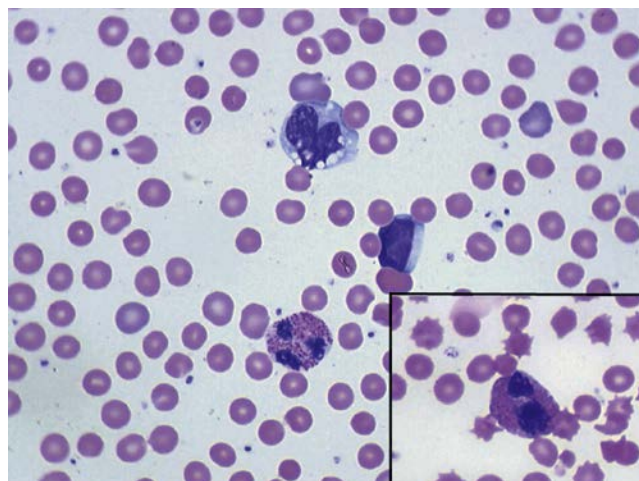


Fig. 39.8 Monocyte, lymphocyte, heterophil (top to bottom), and eosinophil (insert) in the blood smear of a rabbit. (Wright-Giemsa, magnification $\times 1000$)

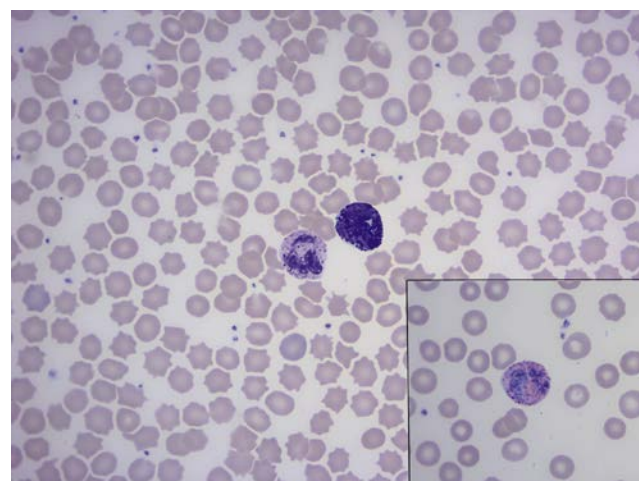


Fig. 39.9 Heterophil showing toxic change (basophilic granules and hypogranulation) (left) and basophil (right) in the blood film of a rabbit. Note the normal heterophil (insert) for comparison. (Wright-Giemsa, magnification $\times 1000$)

closely followed by neutrophils (43%).³⁷ Eosinophil granules are rounder and more numerous than those of neutrophils (Fig. 39.10).⁸⁵ Small and large lymphocytes are reported in ferrets.⁸⁵

Hedgehogs. Leukocyte morphology of African hedgehogs is similar to other domestic carnivores (Fig. 39.11).¹¹ A study of European hedgehogs found that lymphocytes were the predominant leukocyte, and basophils were increased in numbers compared with other species.⁶⁹

Interpretation of Abnormal Leukocyte Parameters

In general, neutrophil/heterophil numbers increase with inflammation associated with invading bacterial microorganisms.¹¹ Similar to other mammals, an acute inflammatory response is characterized by a neutrophilia with increased numbers of bands (left shift) and often a monocytosis.⁶² However,

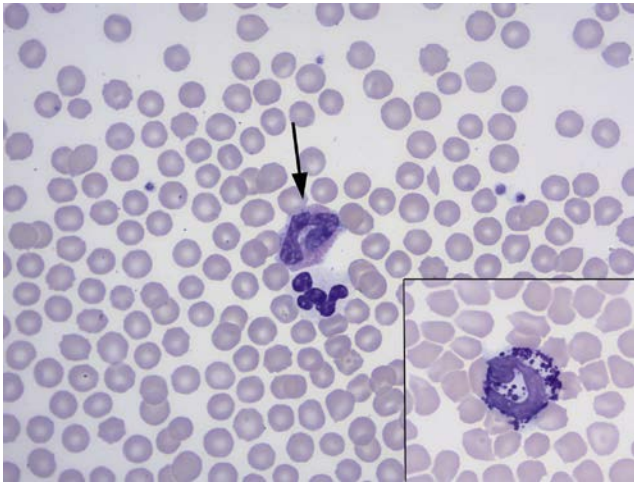


Fig. 39.10 Eosinophil (arrow), neutrophil, and basophil (insert) in the blood film of a ferret. (Wright-Giemsa, magnification $\times 1000$)

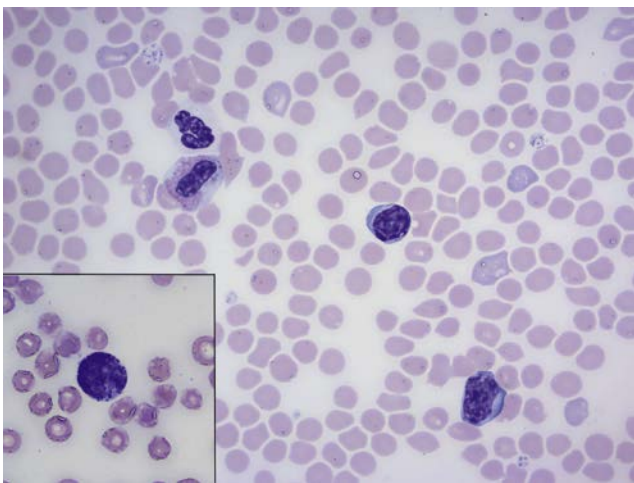


Fig. 39.11 Neutrophil, eosinophil, two lymphocytes (top left to bottom right), and basophil (insert) in the blood film of a hedgehog. (Wright-Giemsa, magnification $\times 1000$)

some small mammals like chinchillas and guinea pigs may have only increased proportions of heterophils (reverse of the normal distribution) without a leukocytosis in early inflammatory stages. Likewise, significant leukocytosis ($>15,000$ cells/ μL) or a left shift is not common in rabbits with acute systemic inflammation.¹⁷ Instead, a leukopenia with a normal differential or a normal WBC count with a heterophil-dominated differential may be observed.⁶² In ferrets, leukocyte numbers above 20,000 cells/ μL and a left shift are not commonly seen with inflammatory disease,¹¹ and chronic inflammation may result in leukopenia.⁸³ In mice and rats, circulating bands are uncommon, and the degree of the inflammatory response is less pronounced; even mild increases in neutrophils may be significant in these species.⁶⁴ Thus, in small mammals, the presence of immature cells like bands and toxic changes or a change in the neutrophil/lymphocyte ratio are more reliable indicators of inflammation than the total WBC and differential counts.¹¹

Illness, handling, or trauma may cause a leukocytosis characterized by a neutrophilia and lymphopenia due to endogenous glucocorticoid release.¹⁷ This may occur simultaneously with

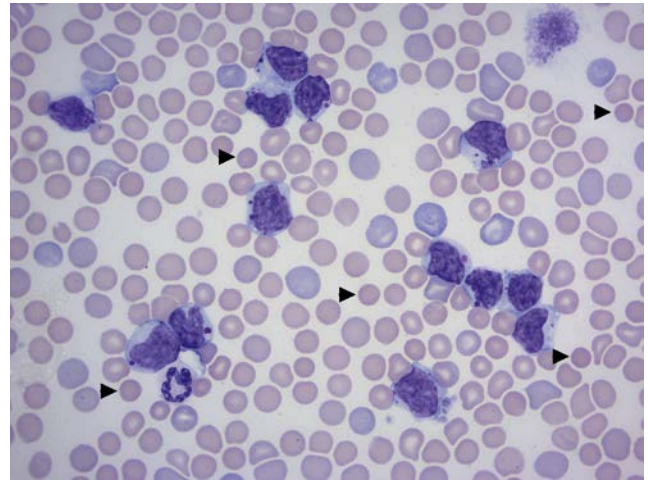


Fig. 39.12 Marked leukocytosis characterized by large granular lymphocytes in a Fisher rat with large granular lymphocyte leukemia. Numerous smaller erythrocytes without a central pallor, spherocytes (arrowheads), and polychromatophilic erythrocytes are also present in the background. (Wright-Giemsa, magnification $\times 1000$)

a compensated inflammatory response, making interpretation difficult. In rats and mice, catecholamine release (fight/flight response) increases both lymphocytes and neutrophils because of the demargination of neutrophils.^{13,64}

Large granular lymphocyte (LGL) leukemia is a common cause of death in aging Fisher 344 rats and has been occasionally reported in Wistar-Furth rats.^{70,75} There is a single report of LGL leukemia in ferrets.⁶ This leukemia likely originates in the spleen and is characterized by large lymphocytes with natural killer activity and prominent cytoplasmic azurophilic granules (Fig. 39.12).^{13,75} In Fisher rats, LGL leukemia is often associated with immune-mediated hemolytic anemia with spherocytosis and reticulocytosis, as well as thrombocytopenia.⁷⁵ Myeloid leukemia is rare in rats.¹³ Canine leukemia (acute lymphoblastic leukemia) occurs rarely in young adult guinea pigs and presents with leukocyte counts that range from 25,000 to 500,000 cells/ μL , lymphadenopathy, and hepatosplenomegaly with neoplastic infiltrates.⁸² Ferrets with lymphoma may have a lymphocytosis and occasionally neutropenia and thrombocytopenia.⁷¹

Similar to other mammals, differential diagnoses for eosinophilia are hypersensitivity responses and tissue parasites rather than parasites in the intestinal lumen.⁷³ Moderate to severe eosinophilia may be seen in ferrets with eosinophilic gastroenteritis or heartworm disease.⁷¹

Monocytosis, usually with neutrophilia or a left shift, generally reflects increased demand of tissue macrophages, whereas a mild monocytosis combined with a mild neutrophilia and lymphopenia may be present with a glucocorticoid response.¹⁰

Neutropenia may result from overwhelming acute inflammatory response (usually with a left shift) or secondary to decreased neutrophil production resulting from primary bone marrow disease.⁶² Leukocyte counts as low as 3000 to 4000 cells/ μL occur in normal ferrets and should not be interpreted as leukopenia.⁷¹

Evaluation of Platelets

Platelets are small (1–3 μm) rounded to oval to elongated, pale, basophilic anucleated cell fragments derived from the cytoplasm of megakaryocytes that prevent bleeding and have a major role in inflammation.³⁴ Compared with other species, platelet counts in mice and rats are higher, with reference intervals as high as 1600×10^3 cells/ μL and 1450×10^3 cells/ μL , respectively.¹¹ Mouse and rat platelets may spontaneously activate or aggregate in response to stimuli, resulting in platelet clump formation.⁶⁴ Therefore platelet counts of rats and mice are often inaccurate due to clumping and the underestimation of platelet counts by some hematologic analyzers because of the small size of rodent platelets.⁶⁴ Thrombocytopenia occurs in female ferrets in estrus as well as in females with hyperestrogenism exhibiting severe anemia and marked thrombocytopenia.⁶⁴

Interpretation of Abnormal Platelet Numbers

Thrombocytopenia is a common laboratory finding in small mammals and is often spurious because of blood collection difficulties and platelet clumping.⁶⁴ Therefore blood smear evaluation and platelet estimation are recommended to confirm low automated platelet counts. True thrombocytopenia may be caused by decreased production (hypoplastic bone marrow) or secondary to destruction or consumption of platelets.³⁴ Marked thrombocytosis, without significant leukocytosis, may be the only evidence of inflammation in some small mammal species like chinchillas.⁶⁷ Iron deficiency anemia due to chronic hemorrhage and accelerated erythropoiesis are other conditions that may result in thrombocytosis.³⁴

BIOCHEMISTRY

Reference Intervals: Test Interpretation

All laboratory data are compared to a “normal” set of values or RIs that are considered representative of health. In the absence of RIs, laboratory data are meaningless. Data interpretation in veterinary laboratory medicine has traditionally used cross-sectional, population-based RIs that can prove problematic in exotic species medicine given the large sample numbers necessary for generating representative RIs. Current recommendations for establishment of RIs ideally require 120 healthy individuals, although 40 is the minimum acceptable number.²⁵ With many exotic pet species, biochemical RIs are lacking, and those that are available may be inappropriate. Using these sets of RIs for test interpretation can be misleading and result in either not detecting or falsely identifying disease states. The risk of clinical misinterpretation of patient values outside of RIs is mitigated if the clinician is fully informed as to how the intervals were generated and therefore how representative they truly are. Selected biochemical values for rodents, rabbits, ferrets, and hedgehogs are available in this and other publications.^{37,38,50,54}

Subject-based RIs derived from longitudinal data may provide a viable alternative to population-based RIs for exotic species.⁷⁸ Subject-based RIs allow data from a sick animal to be compared with values obtained from that individual in health. Changes between two consecutive values in an individual patient can be identified as significantly different by using a reference

change value (RCV) or critical difference value, expressed as a percentage change. The RCVs can be calculated from biological variation data that can be obtained from relatively few animals over time. Once more data on biological variation are published for exotic species, RCVs will be available to assist in data interpretation in the absence of RIs. Nondomestic species with published biological variation data include Dumeril’s monitor lizards, rats, and bald eagles.^{5,14,41}

Preanalytical Variation

Preanalytical variation in small mammals occurs as a result of differences in sampling sites, anesthesia, stress, diet, age, pregnancy, sex, fasted or nonfasted state, and seasonal variation. Information regarding these variables are useful in data interpretation. The more characteristics shared by your sample and the samples used to generate the data for the RI used for test interpretation, the more accurate will be the interpretation. Some known preanalytical effects are listed below.

Blood Collection Site

Test values differ as a result of how the blood sample was obtained. In mice, samples collected from the retroorbital venous sinus have lower concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), protein, albumin, triglycerides, total cholesterol, and creatinine and higher glucose values compared with samples from the submandibular vein.^{16,21} In rats, creatine kinase (CK) and AST concentrations are higher in blood samples taken from the retroorbital sinus than from the heart.⁴ Using a consistent site for blood collection in a given species will help to mitigate the effects of preanalytical variation due to collection site. Different blood collection methods also result in varying degrees of hemolysis, which can cause spurious results for multiple analytes.

Anesthetics

In rabbits, isoflurane and halothane produce changes in some analytes relative to preinduction concentrations. In one study, halothane administration significantly increased serum glucose, ALT, AST, urea nitrogen, and creatinine levels; isoflurane resulted in similar effects, although ALT level was not significantly impacted. In some cases, the increases resulted in values above the population-based RI for rabbits. The effects persisted up to 120 minutes after anesthesia was discontinued.²⁹ Ketamine-xylazine and ketamine-diazepam injections in rabbits caused increases in urea nitrogen and creatinine above the upper limit of the RI up to 24 hours after injection; significant increases in ALT and AST relative to baseline were also reported. In contrast, fentanyl-droperidol sedation produced no effects on the parameters measured (AST, ALT, alkaline phosphatase [ALP], gamma glutamyl transpeptidase [GGT], urea nitrogen, creatinine, phosphate, and potassium).³⁰

Pregnancy

In pregnant New Zealand white rabbits, total protein, albumin, glucose, cholesterol, calcium, urea nitrogen, and creatinine levels decreased significantly during the middle or late periods of gestation.⁵² Relative to nonpregnant females, mean and/or

median RI values for pregnant Wistar Hannover and Sprague-Dawley strains of rats were below the lower limit of the RI for glucose, sodium, and chloride and above the upper limit of the RI for total bilirubin, triglycerides, and cholesterol.⁴⁵

Fasted or Nonfasted

The need to fast species that feed mainly at night is controversial, because a fast contradicts the normal circadian pattern of the rodent. Fasted samples are usually recommended for laboratory analysis to decrease lipemia that can interfere with many laboratory tests. Moreover, lipemia enhances hemolysis, compounding assay interference. In rats, a minimum of 16 hours fasting is necessary to produce a nonabsorptive state characterized by triglyceride, glucose, and ALP concentrations that are significantly lower than nonfasted samples.⁷⁹ The fasted state may mask mild elevations in ALP associated with cholestasis.

Analytical Variation

The importance of test validation for different species cannot be overstated; blood samples should be submitted to veterinary reference laboratories that have validated assays for particular veterinary species. The use of point-of-care biochemical analyzers or handheld glucometers that have not been validated for the species in question will lead to laboratory results of questionable accuracy or poor reproducibility that could affect test interpretation. A methodology that is adequate for one species may be inappropriate for another as a result of interspecies structural differences in any given analyte.⁷⁷ Moreover, assays may not be accurate for some species if reference values for a particular analyte fall below or above the analytical range or detection limit of the analyzer.

Often there are generalized statements about the spurious effects of hemolysis, icterus, or lipemia on biochemical values. Species differences exist in the effects of interferences caused by serum lipid, hemoglobin, or bilirubin on analyte measurements.⁴⁰ Reported interferences may or may not be applicable to the species being evaluated. One cannot assume that hemolysis will universally result in spurious hyperkalemia, for example. For species with high potassium content erythrocytes, this is often true, but erythrocyte potassium content varies considerably between species. Because the effects of hemolysis or lipemia on the accuracy of biochemical tests are unknown in many nondomestic species, avoidance of these interferences is crucial to accurate test interpretation.

Rodents

The CBC and serum biochemical analyses in adult mice and other small rodents requires roughly 10% to 15% of total blood volume. While this amount of acute blood loss is usually well tolerated in healthy animals, taking blood from animals that are already ill can exacerbate dehydration and azotemia and cause significant decreases in body temperature and activity. Pretreatment with intraperitoneal fluid therapy has been shown to mitigate some of the deleterious effects of blood loss in ill mice.⁴⁸ Splitting a blood sample from a single animal into two different tubes for a CBC and biochemical evaluation may result in inadequate sample volume to perform the desired tests or

may introduce inaccuracies if the ethylenediaminetetraacetic acid (EDTA) tube is underfilled. A plasma sample provides more volume relative to serum and can be used for both the CBC and biochemical evaluations. The largest plasma volume can be extracted from a blood sample by using a lithium heparin separator tube with a gel plug.⁸¹ Lithium-heparinized plasma is recommended whenever electrolytes are evaluated, because plasma collected in potassium EDTA or sodium heparin may have inaccurate potassium and sodium results, respectively.

Liver

Mice, hamsters, gerbils, and chinchillas are similar to rats with respect to markers of hepatocellular and hepatobiliary injury and their interpretation. A minimum of two appropriate tests is recommended for hepatocellular evaluation. Hepatocellular tests appropriate in most rodents include ALT, AST, and sorbitol dehydrogenase (SDH).⁷ For hepatocellular evaluation, ALT and SDH are highly specific cytosolic liver enzymes; SDH correlates slightly better than ALT with the presence of histopathologic hepatic lesions. Hepatic causes of increased serum ALT and SDH activity are hepatocellular necrosis, injury, or regenerative/repairative activity. Nonhepatocellular increases in ALT activity may be attributed to muscle injury, which can cause increases in both AST and ALT activity. Generally, levels of AST are higher than ALT when both are concurrently increased with muscle injury.

Aspartate aminotransferase is a cytosolic and mitochondrial-associated enzyme that, because of its presence in cardiac and skeletal muscle, is less sensitive and specific for hepatocellular evaluation. Hepatocellular injury usually results in a greater magnitude of increase in ALT than in AST levels, in part due to AST being bound to mitochondria. Large elevations in AST relative to ALT activity would be interpreted as either severe hepatocellular damage or as muscular, not hepatic, injury. Lactate dehydrogenase (LDH) is less sensitive and specific than AST, and use of LDH as a biomarker for hepatocellular injury is not recommended.⁷

In contrast to other rodents, ALT is neither sensitive nor specific in guinea pigs as a hepatocellular biomarker; SDH is used in lieu of ALT. Because AST is less specific for liver disease than SDH is, AST should ideally be assessed with SDH. If SDH is not an available test choice, AST should be interpreted with CK to exclude muscle injury as a cause of increased AST activity.

Bile acids serve to assess hepatic function.⁴⁷ Bile acids measurement is less sensitive than hepatocellular and biliary enzymes to evaluate hepatocellular injury and cholestasis. Decreases in concentrations of analytes synthesized in the liver, such as glucose, albumin, urea nitrogen, cholesterol, and bilirubin, are highly insensitive in detecting hepatic dysfunction, and many are also nonspecific.

Tests assessing biliary injury include ALP, GGT, and total bilirubin. Pathologic increases in ALP are most often associated with hepatobiliary disease and bone injury. In most species, increases in ALP precede increases in total bilirubin with hepatobiliary disease.⁷ Nonpathologic factors affecting increased ALP concentrations are feeding, fasting, sex, and age. Because intestinal ALP is the predominant source of circulating isoenzyme in rats and mice, serum ALP concentrations

may transiently increase postprandially, whereas they decrease within 8 hours of fasting in males and 16 hours in females.^{42,79} Concentrations of ALP tend to be significantly higher in male rats than in females.^{38,42} In contrast to rats, ALP concentrations in some strains of mice may be significantly higher in females than in males.⁵⁸ Young growing rats and mice have higher ALP concentrations than adults due to bone growth.

In rats, GGT is a canalicular enzyme that is associated with cholestasis, but can also be increased secondary to glucocorticoids. Because most ALP is of intestinal origin, increases in both ALP and GGT provide stronger evidence of biliary disease. Total bilirubin concentrations may be increased as a result of bile retention subsequent to impairment of intrahepatic or extrahepatic bile flow (cholestasis), increased production associated with marked erythrocyte destruction (prehepatic), or altered bilirubin metabolism (e.g., Gunn rats).

Kidney

Urea nitrogen and creatinine will increase with decreases in glomerular filtration, but similar to dogs and cats, these are neither sensitive nor specific tests of renal function in rabbits and rodents. Prerenal causes of increased urea nitrogen are high-protein diet, protein catabolism, dehydration, gastrointestinal hemorrhage, and fever. Creatinine is a more specific biomarker than urea nitrogen, and levels do not tend to increase with protein catabolism or gastrointestinal bleeding, but will increase with dehydration. Creatinine is an end product of muscle metabolism; thus, relatively higher and lower concentrations may be attributable to well-muscled and muscle-wasted animals, respectively. Accordingly, body condition should be considered when interpreting creatinine concentrations. Creatinine can be less sensitive as a marker for decreased glomerular filtration in a poorly muscled or markedly muscle-wasted animal. Creatinine may be determined by either an enzymatic method or the Jaffe method. Values can differ significantly depending on the method used, especially in mice.⁶⁰

Electrolytes

Rodent electrolytes are interpreted as for domestic species. Sodium and chloride typically increase and decrease in tandem. Pure water loss (dehydration) or decreased water intake are common causes of hypernatremia and hyperchloridemia. In rodents, sodium and chloride loss occurs most often from diarrhea, osmotic diuresis (diabetes mellitus), and renal disease. Hypotonic fluid administration or polydipsia may result in dilutional hyponatremia and hypochloridemia. Sodium concentrations have been reported to be slightly higher in mice than in other rodent species, largely based on one study that reported values in mature male C57BL-6J mice to be as high as 174 ± 23 (SD) mEq/L.²² However, a recent study using adult C57BL-6J mice (aged 90–135 days) generated sodium reference intervals of 139 to 155 mEq/L.⁵⁸ Other reports in mice have slightly higher upper limits with reference intervals of 132 to 162 and 155 to 161 mEq/L.⁶⁵

Common causes of hyperkalemia in rodents are acute renal failure, postrenal urinary obstruction, marked tissue necrosis, and rhabdomyolysis. Potassium is often spuriously increased

due to leakage from high potassium-content erythrocytes or marked thrombocytosis. Only species with high potassium-content erythrocytes will have hyperkalemia associated with hemolysis or leakage from erythrocytes during clotting. Rats, mice, and hamsters have high potassium-content erythrocytes, resulting in hyperkalemia associated with hemolysis or leakage from intact erythrocytes during clotting.^{9,19,20} Information for the other species is not available, and whether hemolysis results in hyperkalemia is not known. Marked thrombocytosis may result in sufficient release of potassium during the clotting process to produce hyperkalemia; use of plasma samples will obviate this effect. Spurious hyperkalemia can be avoided by using nonhemolyzed plasma that is immediately spun after collection so that potassium leakage from erythrocytes does not occur. Hypokalemia is often caused by decreased intake or renal or gastrointestinal loss.

Serum phosphorus is principally regulated by the kidneys. Increased dietary intake, decreased glomerular filtration, and increased parathyroid hormone secretion are associated with hyperphosphatemia. Vitamin D oversupplementation and cholecalciferol toxicosis result in hyperphosphatemia and hypercalcemia. As in other species, young mice and hamsters have higher phosphorus concentrations relative to adults due to bone growth.^{9,65} Hypophosphatemia is less common and may be seen with hyperparathyroidism. In dogs, significant transient hypophosphatemia may be associated with respiratory alkalosis caused by panting/hyperventilation; studies are not available to determine whether this applies to tachypneic rodents.

Calcium concentration in serum or plasma represents both ionized and protein-bound calcium; thus, hypoalbuminemia is expected to decrease total calcium. Other causes of hypocalcemia in rodents are magnesium-deficient diets, chronic renal failure, and hypoparathyroidism.⁶⁵ Common differential causes of hypercalcemia are paraneoplastic syndromes, hyperparathyroidism, osteolytic lesions, and hypervitaminosis D/cholecalciferol toxicosis. Hyperproteinemia may also result in increased total, but not ionized calcium concentration.

Protein

Protein may be measured as total protein or divided into its components by electrophoresis. A new capillary methodology for electrophoresis permits evaluation of serum protein fractions with as little as 2 μ L, and it has been shown as a viable alternative to conventional agarose gel electrophoresis for protein electrophoresis in mice, rats, and marmosets.¹⁸ Albumin is measured independently of total protein. Unless electrophoresis is performed, globulin concentrations are calculated values that are the result of subtracting albumin from total protein values.

Total protein can be determined with a chemical reaction (biuret method) or by using a handheld refractometer. Refractometry is a total solids-based protein measurement technique that is influenced by the total dissolved solids in the sample. The light refraction index is converted to total protein either via the refractometer scale or published tables. American medical refractometers are designed by using a conversion factor, and their built-in scales report total protein, *not* total solids. Nonprotein solutes in serum and plasma that contribute to

refraction include electrolytes, lipid, urea, and glucose. Total protein estimates from refractometers may be inaccurate when there is marked hyperglycemia (>600 mg/dL), hyperlipidemia, and azotemia (urea nitrogen 273 mg/dL). Sodium concentrations required to significantly affect a refractometer reading are incompatible with life. Hemolysis and icterus do not cause inaccurate refractometer readings, although hemolysis can result in the loss of a readable demarcation line.²⁷

Interpretation of protein changes in rodents is similar to that in domestic animals. In general, increases in total protein are associated with hemoconcentration or hyperglobulinemia, whereas decreases may be attributable to hypoalbuminemia, hypoglobulinemia, or both (panhypoproteinemia). Panhypoproteinemia is usually caused by acute blood loss or protein-losing enteropathy. Increases in globulin concentration are related to chronic antigenic stimulation or neoplasia (i.e., monoclonal gammopathy). Hypoalbuminemia may be due to glomerular disease, loss or decreased absorption in the gastrointestinal tract, or decreased production due to liver insufficiency.

Glucose and Lipids

In veterinary medicine, blood glucose concentration increasingly is being measured by using portable glucometers. However, accuracy of portable glucometers varies widely in veterinary species (see below, Ferrets). Only portable glucometers that have been validated for a particular species should be trusted for glucose measurement.

Glucose is synthesized by the liver but is influenced by pre-analytical factors and many extrahepatic factors such as hormones (insulin, glucagon, glucocorticoids, epinephrine, and thyroxine); thus it is not a specific indicator of hepatic function. Delayed separation of serum or plasma from blood is a common cause of spurious hypoglycemia and can be mitigated by using collection tubes containing sodium fluoride to inhibit glycolysis. Hypoglycemia may be attributable to fasting, liver insufficiency, and tumors secreting insulin and insulin-like growth factor (i.e., insulinoma, leiomyosarcoma, etc.). In contrast to dogs and cats, induced sepsis in rats did not produce hypoglycemia in one study.¹ Hyperglycemia is associated with diabetes mellitus, stress, blood collection site, anesthetics (see Preanalytical Variation), and certain neoplasms such as glucagonoma, functional adrenocortical tumors, and pheochromocytoma.

In veterinary species, cholesterol and triglycerides are the most commonly assessed lipids. Cholesterol concentrations in health tend to be highest in hamsters relative to other laboratory rodent species. In rats, postprandial hyperlipidemia is common and may be seen in at least a third of unfasted rats; a fast of 16 hours minimum is required to reach a nonabsorptive state.⁷⁹ Pathologic hyperlipidemia is most often attributable to endocrine disorders (diabetes mellitus; hypothyroidism), diet, cholestasis, and nephrotic syndrome; Syrian hamsters with renal amyloidosis and hypoalbuminemia may be hypercholesterolemic.⁹ Thyroidectomy in rats and diabetes mellitus in Chinese hamsters are associated with hypercholesterolemia.^{9,47} Diets high in cholesterol produce hypercholesterolemia in rats, hamsters, and mice.^{9,47,65} Concurrent chronic hepatitis and biliary disease in hamsters are associated with increased cholesterol, likely as a result of cholestasis.⁸

Muscle

Biomarkers of skeletal and cardiac injury include CK, AST, and LDH. In rodents, CK and AST are most often used to assess skeletal muscle injury. Because AST is present in muscle and liver and is less specific than CK for muscle, evaluating AST in conjunction with hepatocellular markers (ALT or SDH) increases specificity and may help to distinguish between skeletal muscle and hepatic disease. Given the small size of the heart relative to the skeletal muscle mass, these enzymes have poor sensitivity for cardiac disease. Cardiac troponin-T and cardiac troponin I are highly sensitive and specific markers for traumatic, ischemic, and toxic cardiac injury, which are validated for use in mice and rats.^{55,56}

Rabbits

Changes in biochemical values in rabbits are generally similar as those as discussed above for rodents. However, some specific analytes have variations in rabbits.

Liver

In the rabbit, ALT is not liver specific although it is used commonly for liver evaluation, whereas SDH is liver specific but the assay is not available in all diagnostic laboratories. Because ALT and AST are present in liver and muscle, concurrent evaluation of CK is helpful in localizing the source of enzyme elevation. Markers of cholestasis include GGT, ALP, and total bilirubin. Blood ALP includes bone isoforms; thus levels are increased in young, growing animals, as well as with bone lesions associated with osteoblastic activity.²⁴

Kidney

Creatinine, urea nitrogen, and phosphorus are of similar sensitivity and specificity as other species as markers for glomerular filtration. A unique feature in the rabbit is the fluctuation of urea nitrogen through the day, with highest concentrations occurring in the late afternoon and evening.²⁴

Electrolytes

Interpretations of sodium, chloride, or potassium abnormalities in rabbits are as in other mammals. Potassium shows diurnal variation in rabbits; highest concentrations occur in the morning and lowest concentrations at night.²⁴ Rabbits are a species with high erythrocyte potassium content, thus hemolysis will produce spurious hyperkalemia. Increased phosphate is often a result of decreased glomerular filtration in rabbits and can be associated with bone disease (healing fractures; metabolic bone disease), muscle trauma, or rhabdomyolysis. Total calcium concentrations in rabbits are higher than in many species. Because intestinal absorption of calcium does not depend on vitamin D if dietary levels are high, high-calcium diets may result in hypercalcemia.⁵¹ Similar to horses, renal failure is associated with hypercalcemia as a consequence of the importance of renal excretion in maintaining calcium balance. Other causes of increased total calcium are lytic bone disease and neoplasia. Total calcium in rabbits is protein-bound, and decreases are observed with hypoalbuminemia. Marked demand for calcium in late pregnancy and early lactation can result in hypocalcemia in does.

Protein

Increases in total protein concentration are associated with hemoconcentration or hyperglobulinemia. Decreases may be attributable to hypoalbuminemia, hypoglobulinemia, or both (panhypoproteinemia). Panhypoproteinemia is usually caused by acute blood loss. A common cause of hypoalbuminemia in pet rabbits is chronic malnutrition (poor diet or severe dental disease), whereas protein-losing enteropathy and glomerular disease are uncommon. Reduced cecotrophy can produce hypoproteinemia, specifically hypoalbuminemia.

Lipids and Glucose

Rabbits have the propensity to develop marked cholesterolemia within days of beginning a high-cholesterol diet.⁵⁰ Both glucose and cholesterol concentrations decrease significantly during the middle or late periods of gestation in pregnant New Zealand white rabbits.⁵²

Rabbits have a constant supply of food in the form of cecotrophs, which precludes obtaining a fasted blood sample. Blood samples taken after 96 hours of food deprivation can show little change in blood glucose levels. Differential causes for hyperglycemia are stress/excitement, hyperthermia, and anesthetics (see Preanalytical Variation). Diabetes mellitus has been reported in laboratory rabbits,⁶⁸ although it appears to be rare in the pet population. Significant increases in blood glucose concentration occur with active signs of stress, and marked hyperglycemia was found to be a poor prognostic factor in non-diabetic ill rabbits.³² Hypoglycemia has been associated with liver insufficiency, insulinoma, and prolonged anorexia.

Muscle

Primary biomarkers for muscle injury are AST and CK. Levels can increase after physical restraint, especially if rabbits are fractious or unfamiliar with handling. Rhabdomyolysis may also result in hyperkalemia or hyperphosphatemia.

Ferrets

Most biochemical parameters in ferrets are interpreted as for dogs and cats, although differences exist in the characteristics of some analytes.

Liver

Hepatocellular biomarkers in ferrets are similar to most species. Although ALT and SDH are sensitive and specific for the liver, ferret erythrocytes are rich in SDH, and marked elevations occur as an artifact associated with hemolysis.⁴⁴ Increases in AST along with ALT concentration are noted in hepatic lipidosis. Little information is available regarding tissue distribution of AST in ferrets, but if present in muscle as with many species, evaluation of AST in conjunction with a specific hepatocellular marker and with CK is useful to distinguish between hepatic and muscular disease.

Biliary markers include total bilirubin, GGT, and ALP. Ferrets possess a bone isoenzyme of ALP, and age-related decreases in ALP are presumably due to the cessation of rapid bone growth as in other species. Cholestasis in ferrets may be associated with increases in total bilirubin, ALP, GGT, and cholesterol. In

general, increased ALP activity is uncommon, and increased total bilirubin concentration is rare. Likely as a result of efficient renal clearance, marked hyperbilirubinemia in the ferret is rarely associated with jaundice, even when total bilirubin is as high as 6.2 mg/dL.³¹

Kidney

Whereas creatinine, urea nitrogen, and phosphate concentrations are inversely related to glomerular filtration in ferrets, creatinine concentrations in health are considerably lower than for most species, and increases are often well within the reference limits of most other small mammals. Similar to other small mammals, increases in urea nitrogen may be nonspecific; creatinine is more kidney specific than urea nitrogen but is affected by dehydration. Increases in two or all three of these indexes are highly supportive of decreased glomerular filtration but do not distinguish between prerenal (dehydration), renal, or postrenal (obstruction) causes.

Electrolytes

Changes in sodium, chloride, phosphorus, and calcium concentrations are interpreted conventionally. Common causes of hyperkalemia in ferrets include acute renal failure, postrenal urinary obstruction, marked tissue necrosis, rhabdomyolysis, and hypoadrenocorticism, which may occur as an iatrogenic complication of bilateral adrenalectomy for hyperadrenocorticism. Causes of spurious hyperkalemia in ferrets are similar to those described in rodents; however, hyperkalemia is not reported with hemolysis in ferrets, suggesting that intraerythrocyte potassium concentration is low in this species.⁴⁴

Protein

Interpretation of protein fractions in ferrets is similar to most species. Two distinctive causes of moderate to marked hyperglobulinemia in ferrets are Aleutian disease virus and systemic coronavirus-associated diseases.

Lipids and Glucose

Hypoglycemia is most often associated with insulinoma in ferrets, especially ferrets older than 4 years of age. Spurious and non-pathologic causes of hypoglycemia include delayed separation of blood from plasma or serum and prolonged fasting (>6 hours). Given the relatively high prevalence of insulinoma in ferrets relative to other small mammals, accurately assessing glucose levels in ferrets is important. The growing attraction of handheld glucometers for glucose measurement is based on ready availability, low expense, and rapid results requiring relatively small amounts of capillary blood. Recent studies illustrate the variability in accuracy for glucose measurement using different glucometers in ferrets and underscore the need for verification with a laboratory analyzer.⁷⁴ Much of this variation may be attributable to species-specific matrix properties such as hematocrit, RBC count, mean corpuscular volume, proportion of glucose bound in RBC versus plasma (species differences), and plasma water content.²⁸ In one study with ferrets, a veterinary glucometer coded for use in dogs correlated best with a laboratory analyzer.⁶¹ Differential causes of hyperglycemia are diabetes mellitus and excitement or

stress. Hyperadrenocorticism in ferrets is not typically associated with hypercortisolemia; thus hyperglycemia is not characteristic of this disease. Transient hyperglycemia may develop after surgical excision of pancreatic islet cell tumors and usually resolves within 1 to 2 weeks.¹²

Common causes of increases in cholesterol and triglycerides in ferrets do not include hypothyroidism and hypercortisolemia, because these diseases are rare in this species. In ferrets, hypercholesterolemia is reported with diabetes mellitus and with marked cholestasis associated with cholelithiasis.³¹

Muscle

Commonly used biomarkers of skeletal and cardiac muscle are CK and AST. With severe muscle injury, ALT may also increase. Although CK and AST appear to be appropriate muscle biomarkers in ferrets, neither are significantly increased in most reported cases of disseminated myofasciitis, which is a multifocal inflammatory myopathy. Increases in ALT have been reported in some of these cases, although whether the increase was due to concurrent suppurative hepatitis or to the myopathy is not clear.²⁶

Cardiac troponin-T (cTnT) is a biomarker for cardiac muscle in the ferret, but its sensitivity in disease has not been adequately evaluated. Increases in cTnT values were associated with cardiac puncture in ferrets, although values were highly variable and a second cardiac puncture did not cause further increases, suggesting that most of the increase was attributable to direct tissue contamination rather than to release of cTnT into blood.⁵⁵

Hedgehogs

The African hedgehog, a nonhibernating species, is the most common hedgehog species kept as a pet in the United States. Most available biochemical and hematologic information is derived from the European hedgehog, and data for juvenile European hedgehogs rescued from the wild were recently published.⁶⁹ Limited RI data have been reported for African hedgehogs,^{54,56a} and until more studies have been done, biochemical data should be interpreted in these species as for omnivorous domestic species.

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